FILE 'HOME' ENTERED AT 15:53:42 ON 04 JAN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS, MEDLINE, CANCERLIT' ENTERED AT 15:55:00 ON 04 JAN 2002

L1	80614	S	GENE THERAP?
L2	224	S	L1 AND CIRRHOSIS
L3	123566	S	LIVER CELL?
L4	32	S	L3 AND RETROVIRAL TRANSDUCTION
L5	0	S	L2 AND L4
L6	5713	S	(KERATINOCYTE GROWTH FACTOR? OR KGF)
L7	68010	S	(TRI-IODOTHYRONINE OR TRIIODOTHYRONINE)
L8	8	S	L6 AND L7
L9	0	S	L8 AND L2
L10	101	S	DIOCTADECYLAMIDOGLYCYLSPERMINE
L11	0	S	L10 AND L4
L12	2	S	L10 AND L8
L13	1	DUP	REM L12 (1 DUPLICATE REMOVED)

l 119 1 ti abs ibib

L13 ANSWER 1 OF 1 MEDLINE DUPLICATE 1

TI Synergistic growth factors enhance rat liver proliferation and enable retroviral gene transfer via a peripheral vein.

AB BACKGROUND & AIMS: Genetic diseases reflecting abnormal hepatocyte function are potentially curable through gene therapy. Retroviral vectors offer the potential for permanent correction of such conditions. These vectors generally require cell division to occur to allow provirus entry into the nucleus, initiated in many experimental protocols by partial hepatectomy. We have explored methods to improve the efficiency of retroviral gene transfer that avoid the need for liver damage. METHODS: **Triiodothyronine** (T3) and **keratinocyte growth factor** (**KGF**) were used to induce hepatic proliferation in rats. The effects of intraportal and peripheral administration of a modified retrovirus that encoded the Lac Z gene during growth factor-induced liver hyperplasia were analyzed. RESULTS: T3 initiated hepatocyte proliferation midzonally; after **KGF**, proliferation was more diffuse. Optimal concentrations of T3 and **KGF** acted synergistically to induce proliferation in 61% of hepatocytes in the intact liver. This enabled in vivo hepatocyte transduction, leading to gene expression by up to 7.3% of hepatocytes after intraportal retroviral vector administration and 7.1% after peripheral venous administration. CONCLUSIONS: T3 and **KGF** act synergistically to induce hepatocyte proliferation in undamaged liver. The liver can be simply transduced with integrating vectors via the peripheral venous system during a wave of growth factor-induced proliferation.

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